B. L. TRUESDELL, T. B. HAMBY, C. S. SEVOV* (THE OHIO STATE UNIVERSITY, COLUMBUS, USA)

General C(sp²)–C(sp³) Cross-Electrophile Coupling Reactions Enabled by Overcharge Protection of Homogeneous Electrocatalysts


Nickel-Catalyzed Cross-Electrophile Coupling using Electrochemistry

\[
\begin{align*}
\text{Ni(η^3-L)OAc (2.5 mol%)} & \\
\text{Ni(η^3-L)₂ (5.0 mol%)} & \\
\text{Ph₃P (0-2.5 mol%)} & \\
\text{KPF₆ or NaI (0.1 M)} & \\
\text{Ni(–)/Zn(+) r.t. or 50 °C, DMA, 2.5 equiv e⁻} & \\
\end{align*}
\]

**Selected examples:**

- \( \text{EtO}_2\text{C} \) \( \text{EtO}_2\text{C} \) \( \text{EtO}_2\text{C} \) \( \text{O} \) \( \text{NBoc} \) 82% yield
- \( \text{EtO}_2\text{C} \) \( \text{OPh} \) 80% yield
- \( \text{MeO} \) \( \text{O} \) \( \text{MeO} \) \( \text{NBoc} \) 95% yield
- \( \text{EtO}_2\text{C} \) \( \text{Cl} \) 98% yield
- \( \text{EtO}_2\text{C} \) \( \text{OPh} \) 83% yield
- \( \text{MeO}_2\text{S} \) \( \text{NBoc} \) 93% yield
- \( \text{MeO}_2\text{S} \) \( \text{Cl} \) 91% yield
- \( \text{MeO}_2\text{S} \) \( \text{OPh} \) 81% yield
- \( \text{MeO}_2\text{S} \) \( \text{CN} \) 98% yield
- \( \text{EtO}_2\text{C} \) \( \text{Me}_2\text{N} \) 89% yield
- \( \text{EtO}_2\text{C} \) \( \text{CN} \) 80% yield
- \( \text{OPh} \) 53% yield
- \( \text{OPh} \) 81% yield

**Synthesis of pridopidine:**

1. TFA, CH₂Cl₂, r.t., 12 h 82% yield
2. MeCN, reflux, 16 h 98% yield

**Significance:** The authors describe a general nickel-catalyzed cross-electrophile coupling of functionalized alkenyl, aryl, and heteroaryl halides with various primary and secondary bromides using electrochemistry. The alkylated products were obtained in high yields.

**Comment:** Key for high coupling yields was the use of the electron shuttle reagent Ni(η³-L)₂, which efficiently prevents over-reduction and thus decomposition of the unsaturated halides. Significantly, this enables an easy scale up by performing the reaction at high currents on a 75 mmol scale.